



Farming, Food and Health. **First**

Te Ahuwhenua, Te Kai me te Whai Ora. Tuatahi



Putting the sheep SNP50 Beadchip to work: case studies in gene mapping and genomic selection

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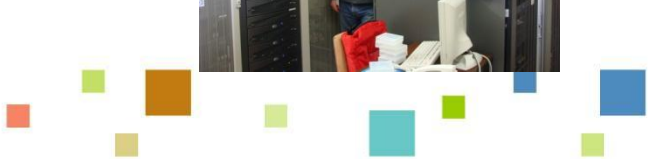
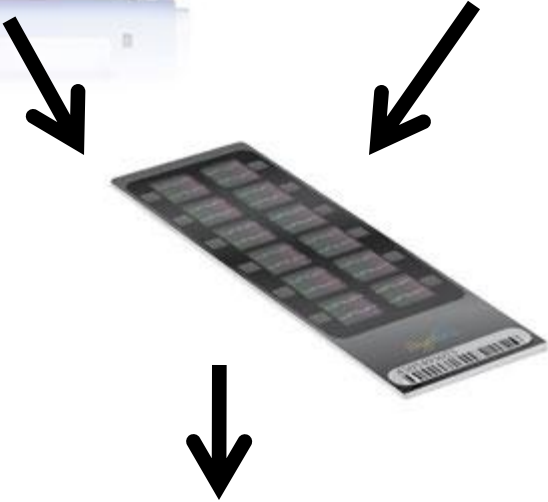
AgResearch & University of Otago

PAG Jan 2010



Overview

- Industry
- GWS
- Major Genes
- Industry



Productivity comparison

	1990-91	2006-07	
Lambing Percentage (ewe)	101.6	117.9	(122% usual)
Hogget lambs as % all lambs	-	3.5	
Average Lamb Wt (kg)	14.35	16.90	+17%
Lamb sold Kg/Ewe	9.76	16.83	+72%
Wool kg/head	5.28	5.60	+6%
Average Steer Wt (kg)	297	320	+8%
Milksolids per cow (kg)	260	325	+25%

Source M&WNZ



Genetic progress: period & flock type

year	\$ Terminal	\$ Dual
1990-94	0.37	0.25
1995-1998	0.34	0.29
1999-2003	SIL 0.61	0.59
2003-2006	CPT/ACE 0.83	0.92

Nimmo Bell : return on levy

SIL 16.3
CPT ACE 18.4

Potential existing technology ~\$1.40 but we can do better.... ~\$2.00



The future: Whole genome selection (WGS)

- Major advance
- Genome sequencing & SNP chips
 - = “genome wide selection”
- As accurate as progeny testing,
 - but can be done at birth
- Suitable for
 - sex limited,
 - difficult to measure traits or
 - traits measured late in life
- Dairy cattle:
 - increase genetic gain 50-70%
 - while decreasing progeny testing costs
- Application in sheep is still being explored



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5 steps to whole genome selection in NZ

- Sequence & ID SNPs (ISGC)
- Create SNP chip (ISGC)
- Collect DNA
 - from measured animals (progeny tested sires)
 - Genotype
- Create “SNP product”
 - Estimate coefficients
 - Validate
- Use to estimate GBVs
 - $GBV = a*EBV + b*MBV$

3X coverage 6 sheep
Dec 2007

Create and validate 60K SNP chip
Aug 2008

Genotype first resources
Dec 2008

Validate
Oct 2009

1st SNP Product
early 2010



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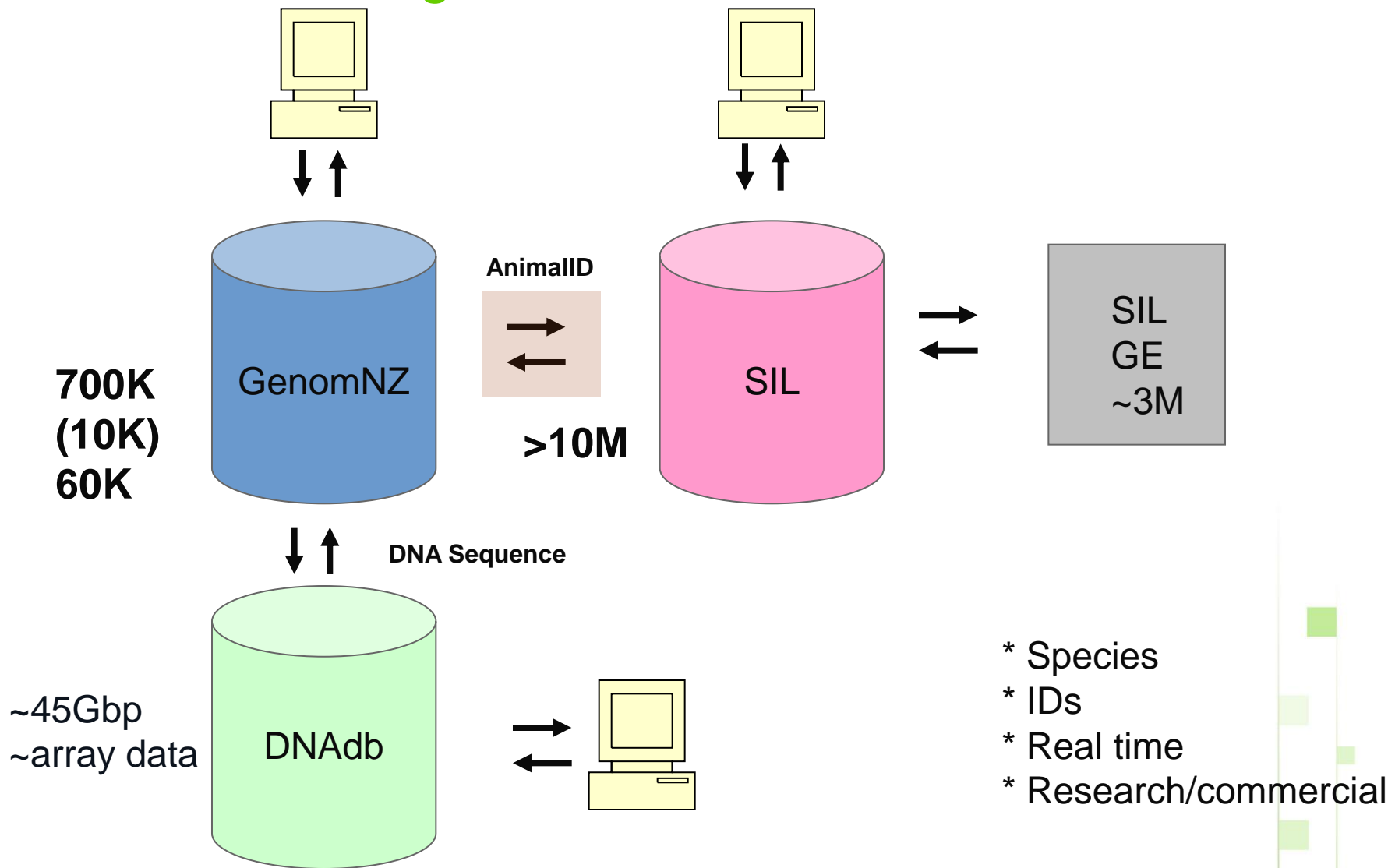
- Ovita owned by M&WNZ & AgResearch
- DNA genomics in sheep
- Industry good outcomes
- First right of refusal to Pfizer for commercialisation
- First 5 years developed and commercialised 5 DNA tests
- 2009 one new test Polled
- Next year 1st genomic selection tests



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Current NZ AgR/SIL Database structure



Traits

- Top traits include:

- A

- NLB and twinning
- Lamb survival
- Weaning weight (maternal + direct)
- Carcass
- Wool weight

- B

- Adult live weight
- Parasites
- Meat yield (B/C)
- Dags/flystrike/breec score (B/C)
- FE (B/C)
- Longevity
- Fibre diameter

- C

- Feed efficiency
- GHG
- Meat quality



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What NZ animals?

- **Experiment 1 (Jan 2009) n=3000**
 - 2034 industry sires (Rom, Coop, Peren, Composite)
 - Av 43 FEC measured prog/sire
 - Av 187 weaning records/sire
 - Traits: **WWT**, **LW8**, **FWT**, **NLB**, **FEC**, **SUR**, **ULT**, **dags**, **FE..**
 - 693 FEC validation animals, 259 controls (duplicates, mapping, breed standard)
- **Experiment 2 (May 2009) n=2500**
 - FE resistance (Rom, Coop, Composite)
- **Experiment 3 (May 2009) n=460**
 - industry sires used 2008
- **Experiment 4 (Mar 2010) n=3500**
 - 2000 animals meat yield
 - 1500 additional sires and validation animals



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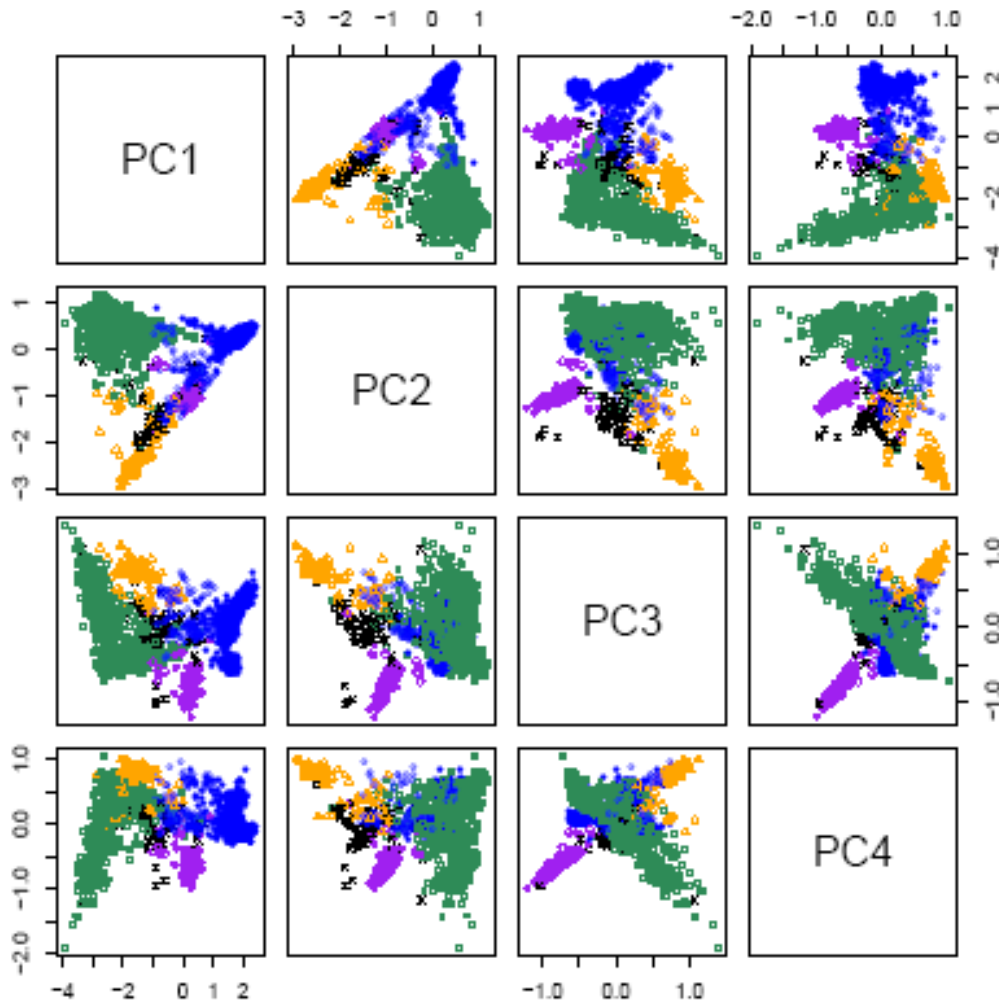
Prelim results: Data QC and method

- Standard genotype checks: final 47,676 SNPs
- Data obtained from SIL BV analysis ~2.5M records
- Converted to adjusted records (Mrode and Swanson 2003)
- R, C, P >50% breed included in training analysis
- Those with phenotype reliability 80% of heritability retained
- Broken into training and validation sets based on birth year
- Used BLUP methodology and adjusted for first 6 breed PCA components
- Validation animals estimates based on own plus progeny records...

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PCA plots



Key (for both plots)

- Romney
- Coopworth
- ◇ Perendale
- △ Texel
- × Marshall Romney
- × Other

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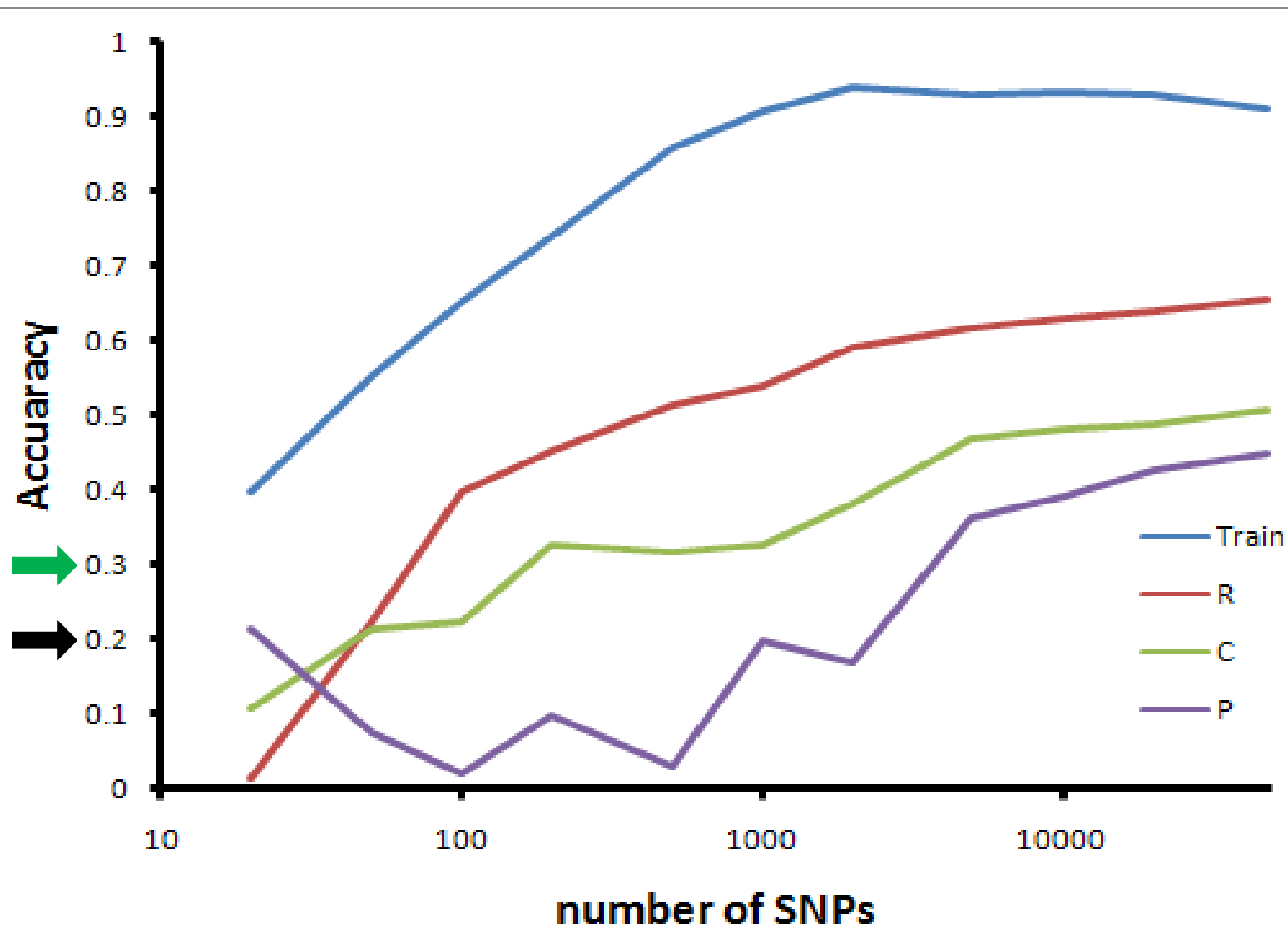
Cut off years and number of animals in training and validation sets.

<i>Trait</i>	<i>1st validation year</i>			<i>nTrain</i>				<i>nValidation</i>			
	<i>R</i>	<i>C</i>	<i>P</i>	<i>R</i>	<i>C</i>	<i>P</i>	<i>Comp</i>	<i>R</i>	<i>C</i>	<i>P</i>	<i>T</i>
<i>wwt</i>	2006	2007	2004	1080	539	116	27	287	252	113	85
<i>cw</i>	2006	2007	2004	1082	538	116	27	286	252	111	85
<i>NLB</i>	2004	2002	2003	690	214	83	6	208	179	62	44
<i>Fec1</i>	2005	2007	2004	664	456	114	26	303	252	109	52
<i>Fec2</i>	2005	2007	2004	654	459	114	26	278	252	107	51
<i>AEFec</i>	2005	2002	2004	594	190	114	8	227	153	101	40

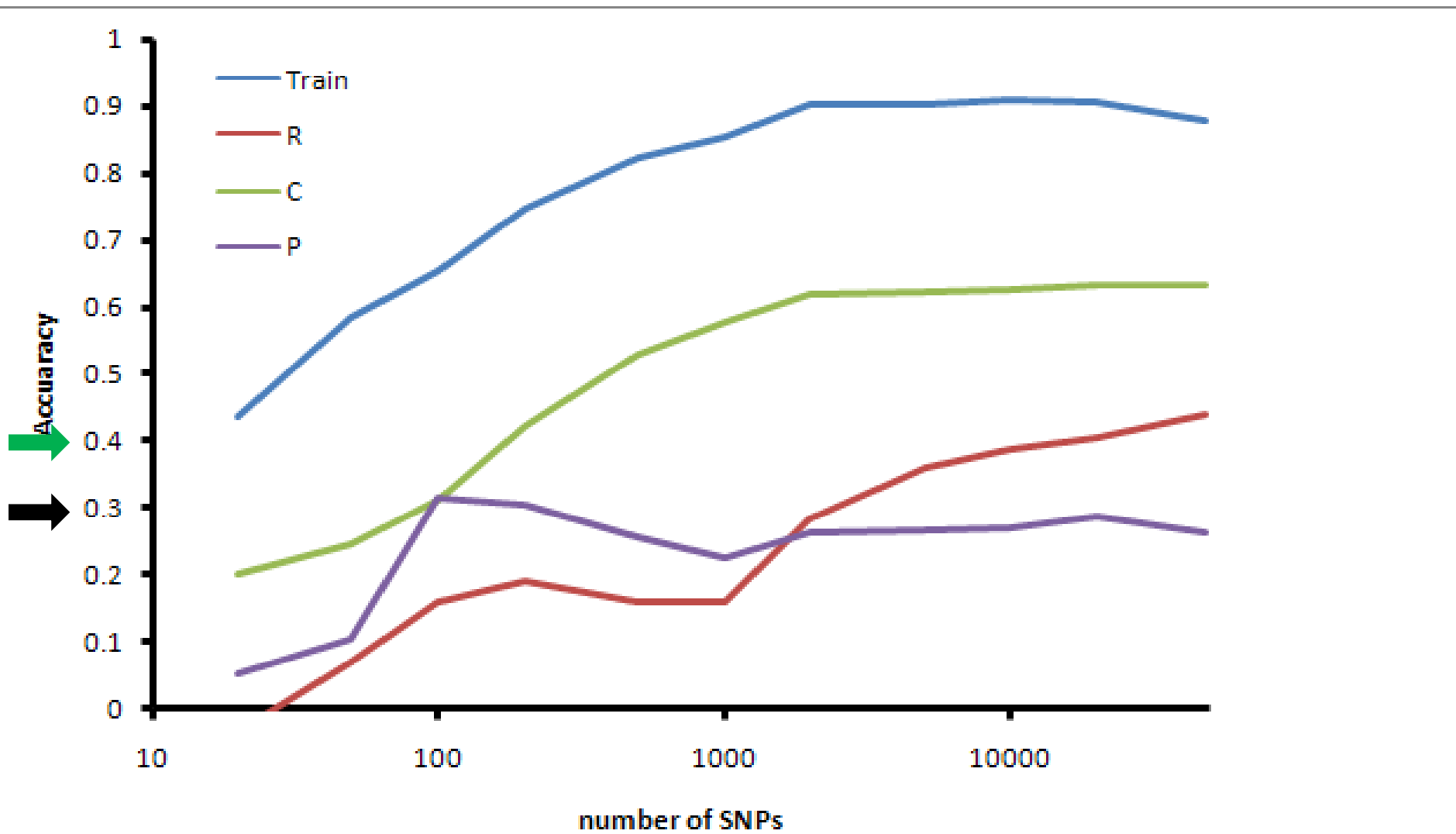
2917 animals in total



WWT

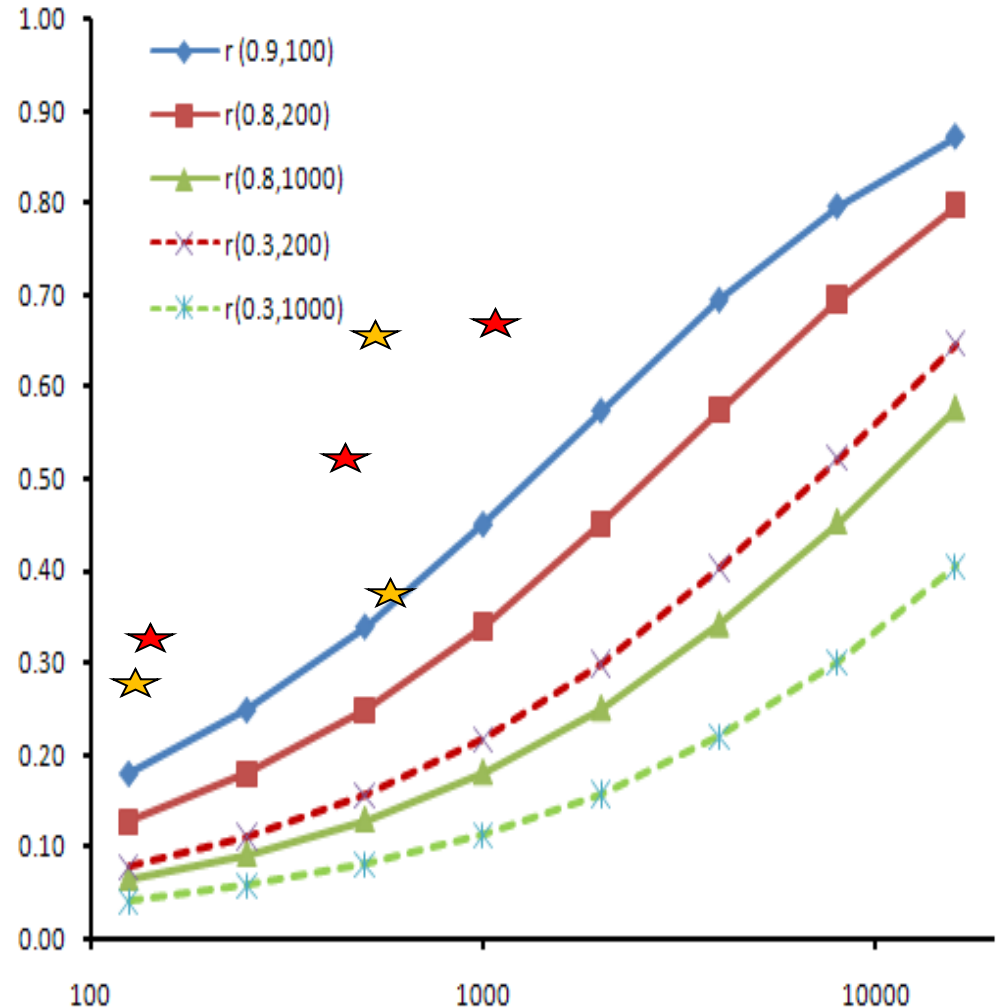


FEC1

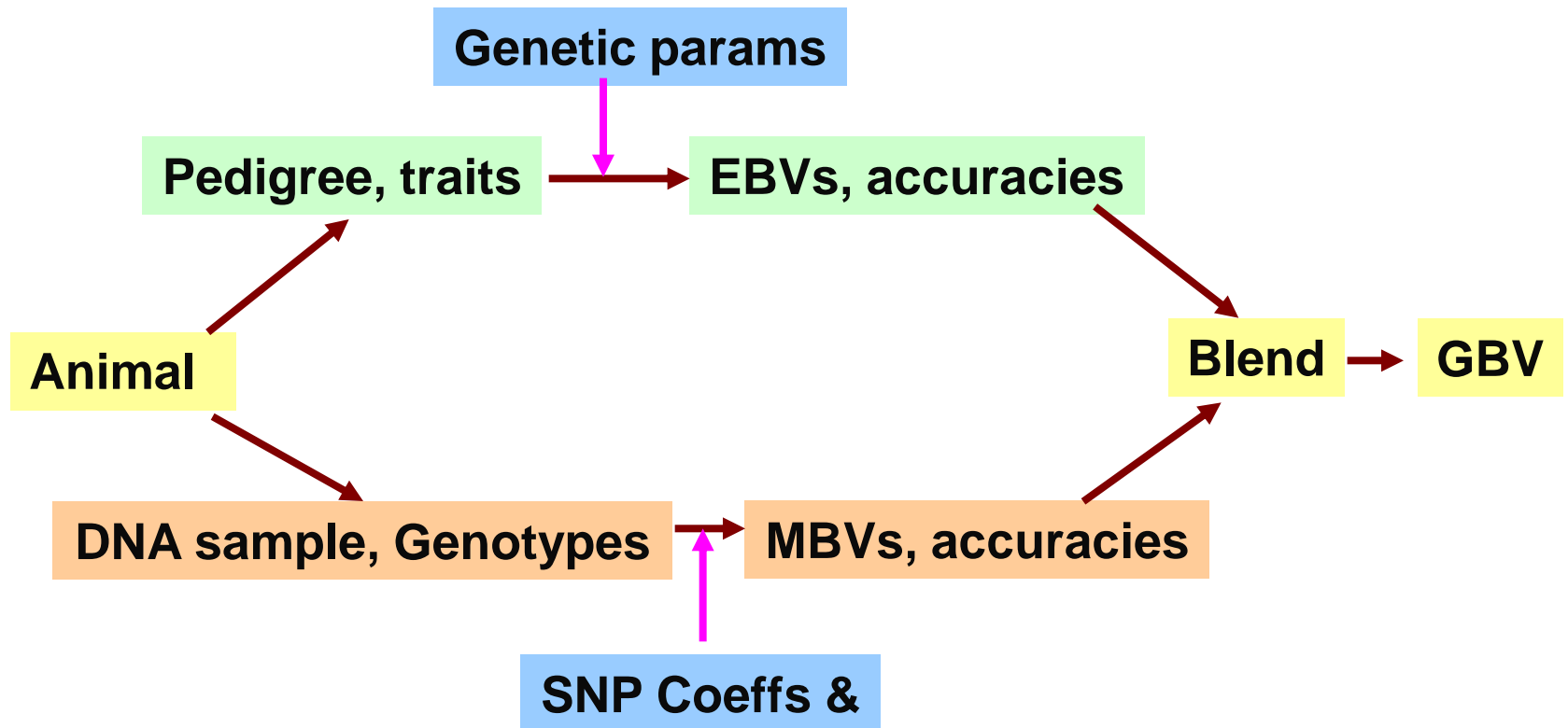


What do we expect?

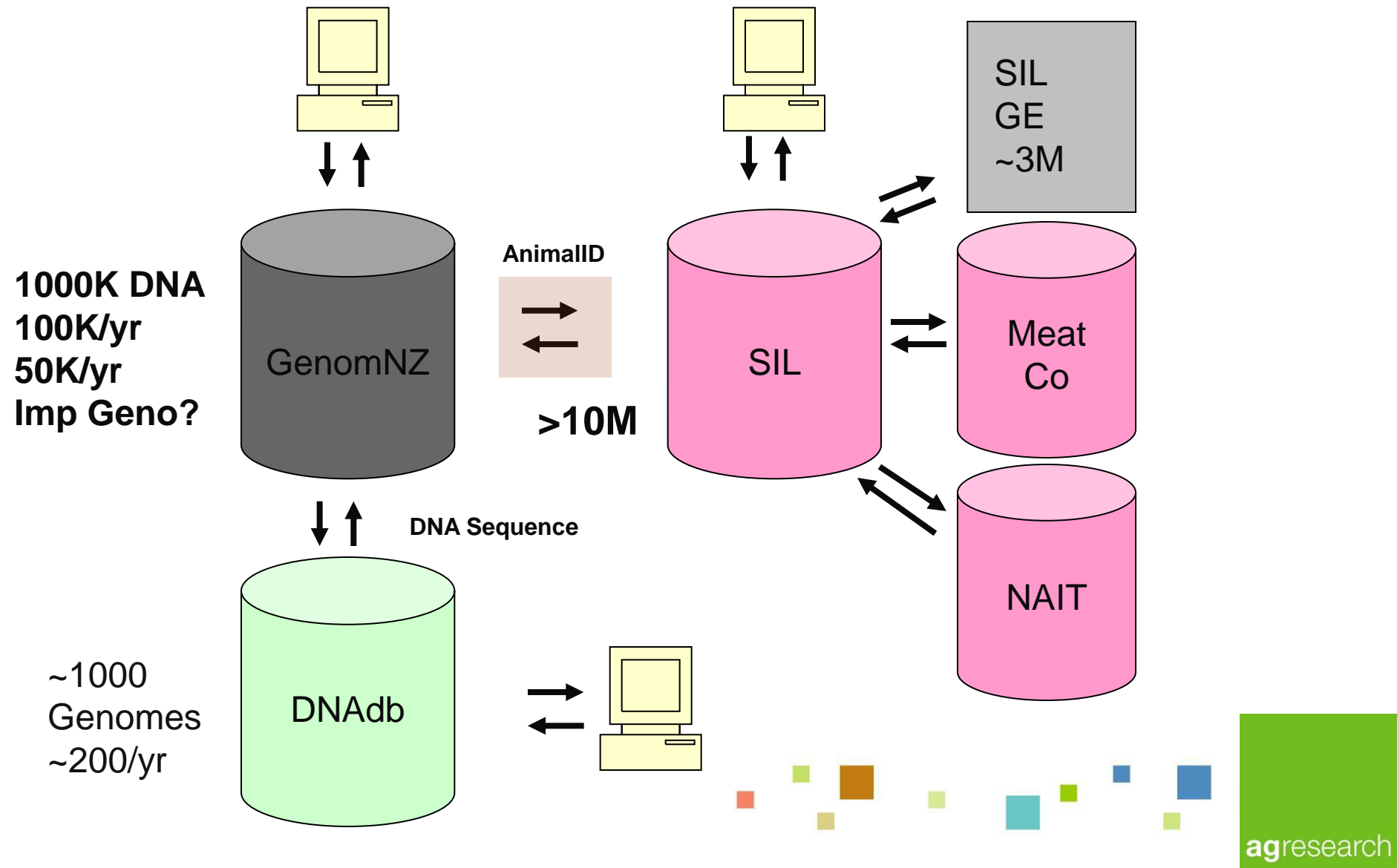
- SNP density
 - $2 \cdot N_e \cdot L$
 - $\sim 30,000$
 - $R_{om} \sim 450$
- Accuracy depends on
 - N_e
 - Effective h^2
- Across breed predictions
 - Need more SNPs
- Need more animals preferably progeny tested sires



SIL Implementation



Future NZ AgR/SIL Database structure



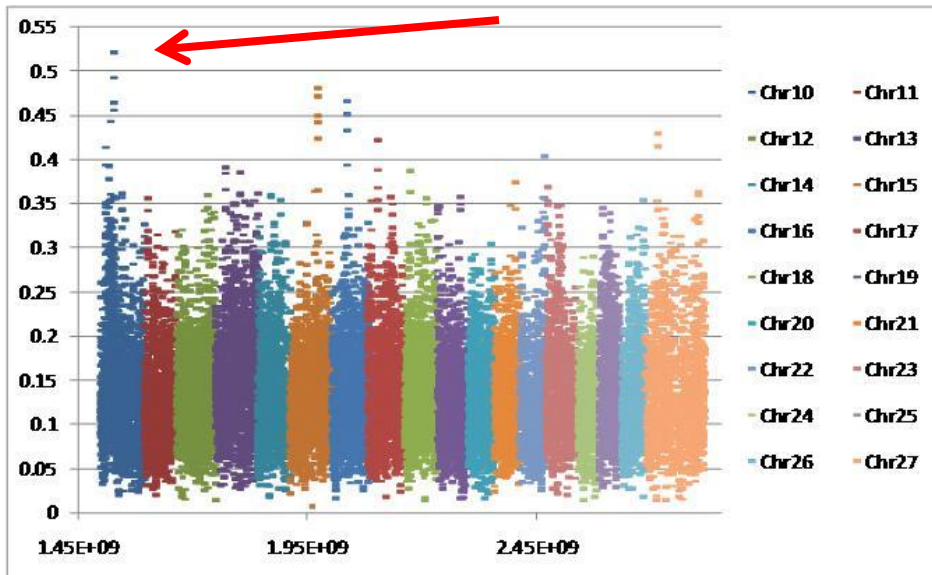
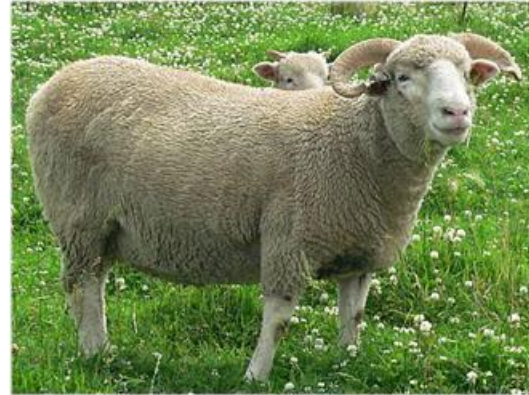
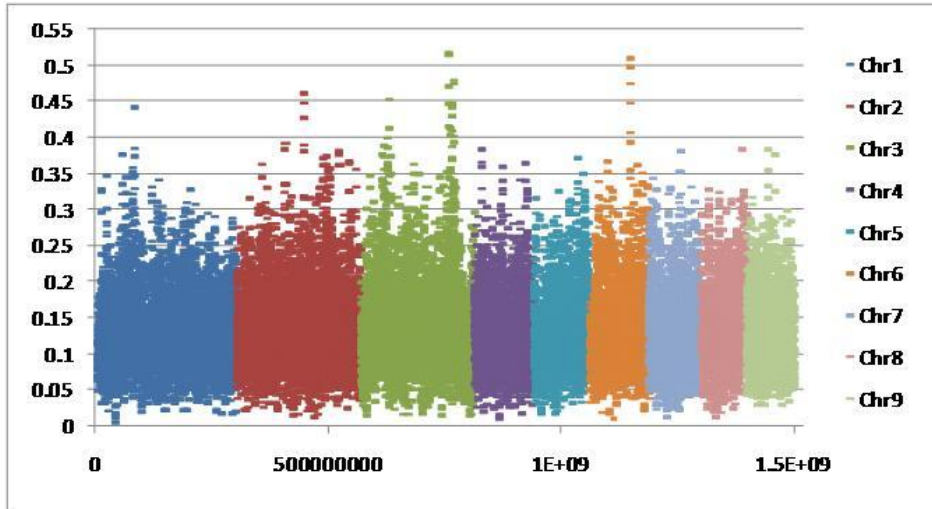
SNP chips: single gene traits

- Very powerful only need 10-15 affected animals for a recessive trait
- Already used in sheep to map
 - SMA
 - “dwarf Texels... Ireland and NZ”
 - Polycystic kidney disease
 - Microphthalmia
 - MyoMax
 - Horns/poll
 - Yellow fat
 -
- Easily added to genomic selection tests

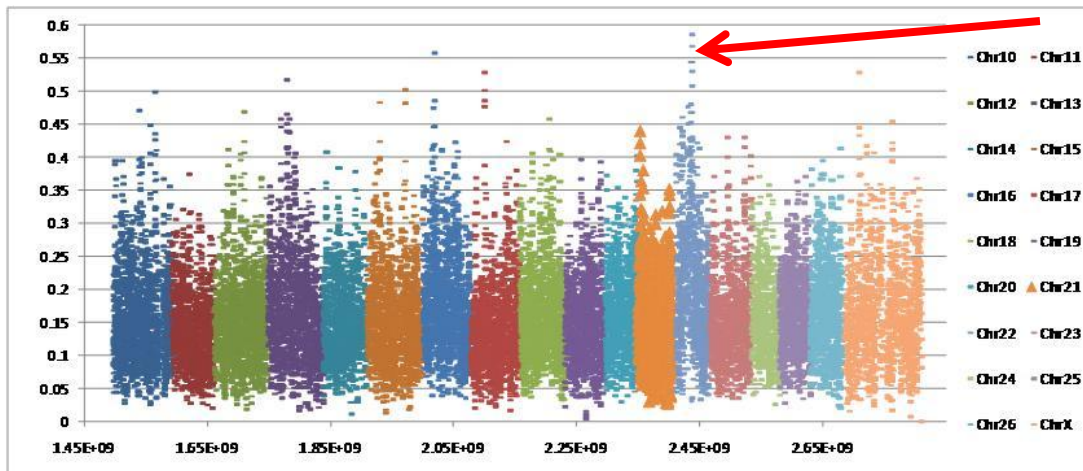
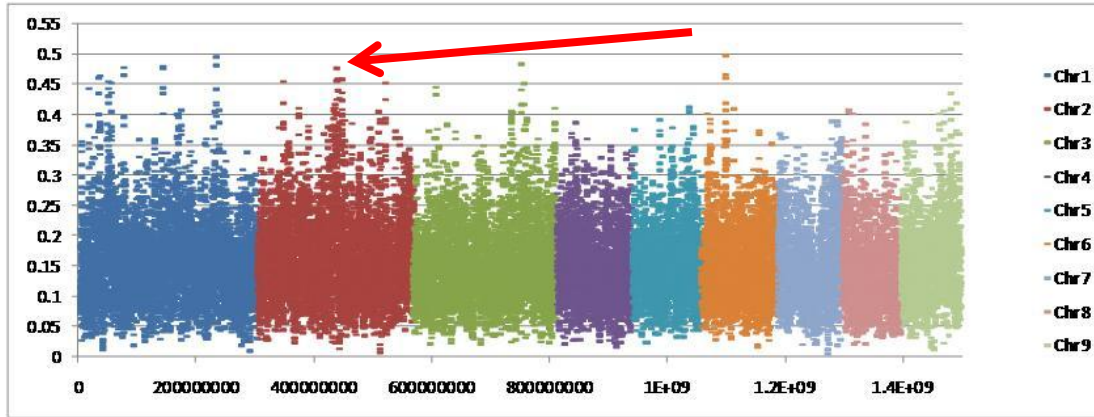
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1. Sheep Domestication: Poll



2. Breed and Trait Specific: meat, microphthalmia



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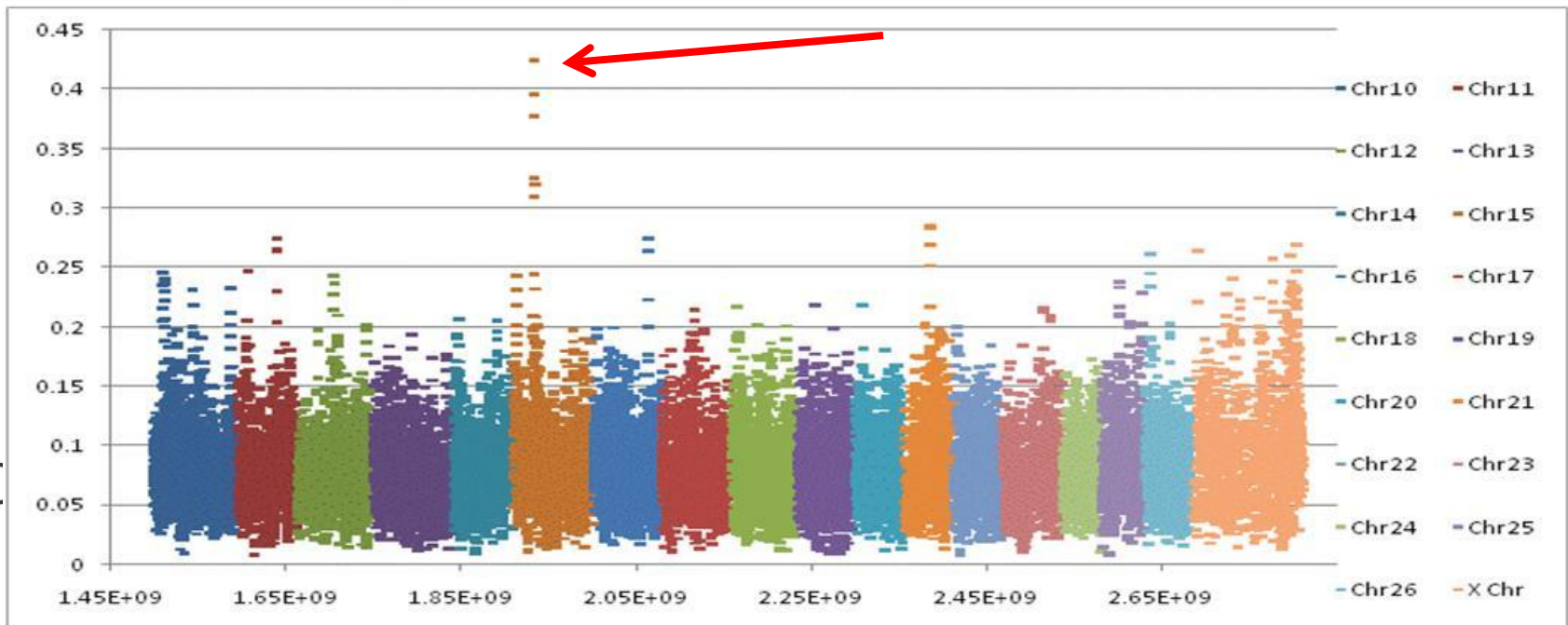
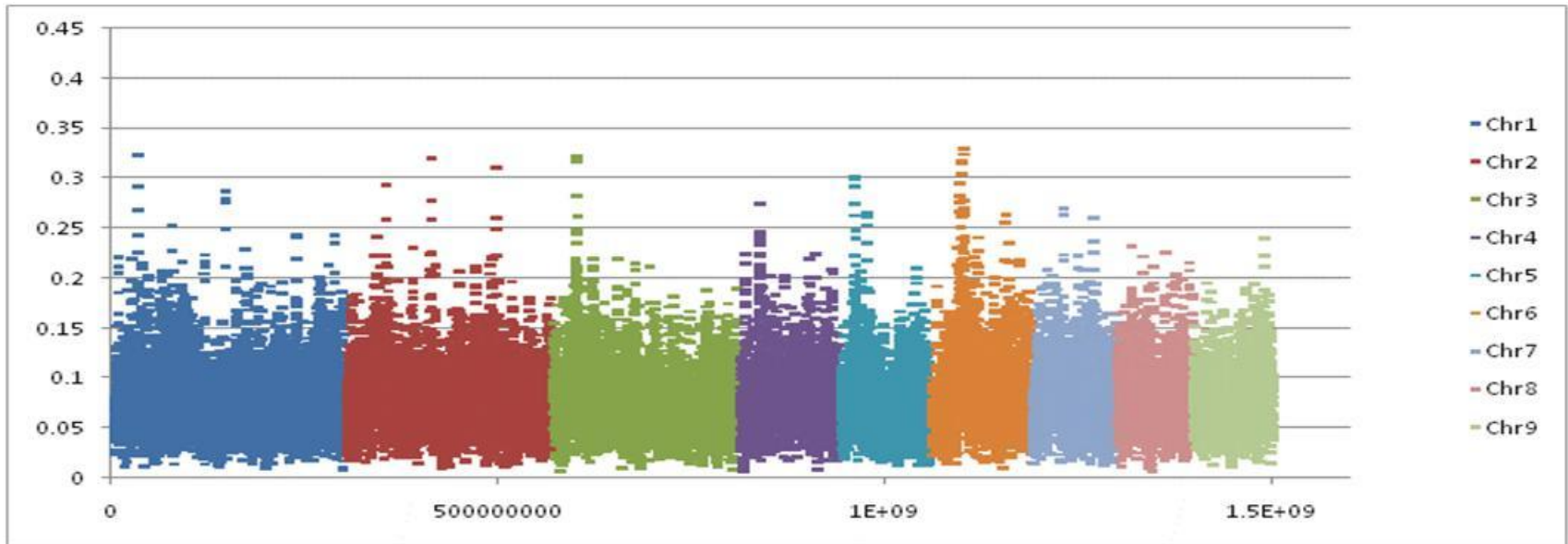


3. Single mutation

- Related to a specific recessive mutation
 - Yellow fat in Perendales
 - Northern Europe origin
 - Carcasses downgraded
 - Partially recessive?



Cases Vs Controls



Summary

- Created ovine chip, genotyped animals, analysed initial results
- Looks like can predict across 3 breeds and crosses.....
- 50K sire product
- More progeny tested sires will improve predictions
- Starting with WWT, CWT, NLB and FEC
 - Have other traits
 - FE already genotyped
 - Meat yield and Survival this year?
 - Excellent for finding single gene traits
- Results SAME FORMAT as existing breeding values

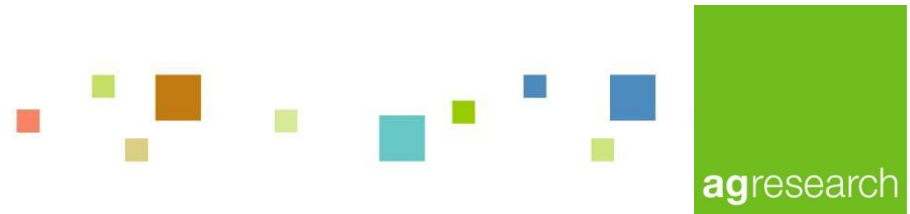
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Acknowledgements

- Ovita
- Meat & Wool New Zealand
- ISGC
- New Zealand sheep breeders

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Animal Genomics Te Anau, June 2006



An example

$$\mathbf{GBV} = \left((1 - \text{Rel}_{\text{pheno}}) \mathbf{MBV} + (1 - \text{Rel}_{\text{markers}}) \mathbf{BV} \right) / (1 - \text{Rel}_{\text{pheno}} * \text{Rel}_{\text{markers}})$$

Trait	Markers		Phenotype		Blended	
	MBV	Acc	BV	Acc	GBV	Acc
animal 1 WWT	1.10	0.45	2.00	0.80	2.29	0.82

- BVs are shrunken
- GBVs have higher accuracies
- More accurate BVs more extreme values
- Not just “adding together”

An example

$$\mathbf{GBV} = \left((1 - \text{Rel}_{\text{pheno}}) \mathbf{MBV} + (1 - \text{Rel}_{\text{markers}}) \mathbf{BV} \right) / (1 - \text{Rel}_{\text{pheno}} * \text{Rel}_{\text{markers}})$$

	Trait	Markers		Phenotype		Blended	
		MBV	Acc	BV	Acc	GBV	Acc
animal 1	WWT	1.10	0.45	2.00	0.80	2.29	0.82
animal 2	WWT	1.10	0.45	0.50	0.30	1.43	0.51

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An example

$$\mathbf{GBV} = \left((1 - \text{Rel}_{\text{pheno}}) \mathbf{MBV} + (1 - \text{Rel}_{\text{markers}}) \mathbf{BV} \right) / (1 - \text{Rel}_{\text{pheno}} * \text{Rel}_{\text{markers}})$$

	Trait	Markers		Phenotype		Blended	
		MBV	Acc	BV	Acc	GBV	Acc
animal 1	WWT	1.10	0.45	2.00	0.80	2.29	0.82
animal 2	WWT	1.10	0.45	0.50	0.30	1.43	0.51
animal 2	NLB	0.17	0.40	0.20	0.20	0.33	0.43

- BVs are shrunken
- GBVs have higher accuracies
- More accurate BVs more extreme values
- Not just “adding together”